

**Amendments to the Specification:**

Replace the paragraph beginning at page 1, line 3, with the following paragraphs:

This application claims full benefit of United States Provisional Application No. 60/198,489, filed April 18, 2000, and French application FR 00 01980, filed February 17, 2000.

The present invention relates to compositions and methods which can be used for regulating the activity of parkin. It relates in particular to a novel protein, referred to as PAP1, which is a partner of parkin, as well as to the peptides or polypeptides which are derived from or are homologous to this protein. It also relates to compounds which are capable of modulating, at least partially, the activity of parkin, in particular of interfering with the interaction between parkin and PAP1. The present invention can be used in the therapeutic or diagnostic areas, or for forming pharmacological targets which make possible the development of novel drugs.

Replace the section "Legends to the Figure" beginning at page 19, line 9, and ending at page 20, line 4, with the following amended section:

**LEGENDS TO THE FIGURES**

Figure 1: Representation of the vector pLex9-parkin (135-290)

Figure 2: Results of the first 5'-RACE experiment. 8 clones were obtained. The initial sequence is indicated on the lower part of the figure.

Figure 3: Results of the second 5'-RACE experiment. Only two of the 8 clones obtained in the first experiment were validated (clones A12 and D5). The initial electronic sequence is indicated below the figure. The complete sequence of DNAs and proteins is provided in Sequences 12-15 (SEQ ID NO: 12-15).

Figure 4: Detailed view of the organization of clones C5 and D4 from the second 5'-RACE experiment. The resulting consensus sequence is indicated on the upper part of the figure.

Appl. No. 09/785,548

Reply and Amendment dated Aug. 20, 2003

Reply to Office Action of Feb. 20, 2003

Figure 5: Structure of transcripts isolated from human brain.

Figure 6: LY111 (full length) nucleic acid (SEQ ID NO: 47) and protein (SEQ ID NO: 48) sequence of human brain. Double underlined: cysteines retained from domain in zinc finger. Bold: Domain C<sub>2</sub>1. Italic: domain C<sub>2</sub>2.

Figure 7: LY111 (short version) nucleic acid (SEQ ID NO: 49) and protein (SEQ ID NO: 50) sequence of human brain. Double underlined: cysteines retained from domain in zinc finger. Bold: Domain C<sub>2</sub>1. Italic: domain C<sub>2</sub>2.

Figure 8: Location of short (8b) or full length (8a) LY111 protein after expression in Cos-7 cells.

Figure 9: LY111 (full length) nucleic acid (SEQ ID NO: 12 or 42) and protein (SEQ ID NO: 13 or 43) sequence from human lung.

Figure 10: LY111 (short version) nucleic acid (SEQ ID NO: 14 or 44) and protein (SEQ ID NO: 15 or 45) sequence from human brain.

Replace the paragraph beginning at page, 26, line 8, with the following amended paragraph:

The 468 bp-fragment of DNA corresponding to the 156 amino acids of the central region of parkin (SEQ ID NO: 4), which begins at amino acid 135, was obtained by PCR using the oligonucleotides (sequence SEQ ID NO. 5 and No. 6), which also made it possible to introduce the *EcoRI* site at the 5' end and a stop codon and a *BamHI* site at the 3' end. The PCR fragment was introduced between the *EcoRI* and *BamHI* sites of the multiple cloning site of the plasmid pLex9, downstream of the sequence encoding the protein LexA, in order to produce the vector pLex9-parkin (135-290) (Fig. 1).

Replace the paragraph beginning at page 34, line 5, with the following amended paragraph:

In order to confirm the presence of a full-length Ly111b transcript in the human brain, a PCR was performed from complementary DNA taken from human fetal brain (Marathon Ready cDNA, Clontech), by using the oligonucleotides LyF1 (AAT GGA AGG GCG TGA CGC, Figure 5, SEQ ID NO. 38) and HA71 (CCT CAC GCC TGC AAC CTG, SEQ ID NO. 39) as primers. A DNA fragment with low representation of approximately two kilobases was amplified. The product of this first PCR served as a matrix for a nested PCR, carried out with oligonucleotides LyEcoF (GCACGAATC ATG GCC CAA GAA ATA GAT CTG, SEQ ID NO. 41) and HA72 (CTG TCT TCG TAT TTC TCC GCC TTG, SEQ ID NO: 41). The amplified products were digested with the restriction enzymes *EcoRI* (integrated into the oligonucleotide LyEcoF) and *BstEII* (Figure 5) and inserted into the expression vector pcDNA3, then their sequence was determined. Analysis of the clone sequences obtained revealed the presence of two potential full-length Ly111b transcripts in the human fetal brain (Figure 5). The first of these transcripts (Ly111b<sub>fullA</sub>) corresponds to the mRNA which was identified in the human lung (Example 6) and encodes a 609 amino acid protein (pLY111b<sub>fullA</sub>; Figures 5,6, SEQ ID NO. 42-43). The second (LY111b<sub>fullB</sub>)

probably represents an alternative splicing product of a common primary mRNA. In this transcript, which is identical to LY111b<sub>fullA</sub>, the sequence between the nucleotides 752 and 956 of the sequence validated in the human lung is absent (SEQ ID NO. 42). LY111b<sub>fullB</sub> thus encodes a 541 amino acid protein (pLY111b<sub>fullB</sub>) (SEQ ID NO: 50) which is identical to pLY111b<sub>fullA</sub> (SEQ ID NO: 48), in which, however, the domain included between amino acids 172 and 240 (Figures 5,7, SEQ ID NO. 44-45) ~~comes to be~~ is missing. The two proteins pLY111b<sub>fullA/fullB</sub> integrate into the domain of interaction with the fragment of parkin which comprises amino acids 135 to 290, which were identified in the yeast (initial sequence LY111b, Figure 5), and can therefore theoretically maintain this interaction.